REMARKS

Upon entry of this Amendment, claims 32-35, 37-46, and 48-51 constitute the pending claims in the present application. Claims 36 and 47 have been cancelled. The subject matter of claim 36 has been included in claim 32, and the subject matter of claim 47 has been included in claim 42. Applicants reserve the right to file a continuing application directed to the subject matter of the cancelled claims.

Claims 32, 37, and 42 have been amended. Support for the claim amendments can be found throughout the specification and original claims. Support for claim 32 is found, for example, on page 3, lines 1-6; support for claim 37 is found, for example, on page 9, lines 21-25; and support for claim 42 is found, for example, in original claim 1 and on page 10, lines 1-9. Further, these claim amendments are fully supported by the working example (pages 21-23) and Figure 4 as originally filed. No new matter has been introduced.

Applicants respectfully request reconsideration in view of the following remarks. Issues raised by the Examiner will be addressed below in the order they appear in the prior Office Action.

Withdrawn Objections/Rejections

Applicants note that the Examiner has withdrawn the Tuschl rejections under 35 U.S.C. § 102(b) and 35 U.S.C. § 103(a) in view of Applicants' amendments and arguments.

Claim Rejections Under 35 U.S.C. § 112, First Paragraph

Claims 32-51 are rejected under 35 U.S.C. § 112, first paragraph, as containing subject matter that is allegedly not adequately described in the disclosure in a way that conveys to one skilled in the art that the applicant possessed the claimed invention at the time the application was filed. Applicants respectfully traverse this rejection to the extent it is maintained over the claims as amended.

Specifically, the Examiner states that the number of claimed nucleic acid sequences is very large and that the vectors are of any origin and can infect cells of any type via any mechanism using any snRNA with any restriction enzyme. The Examiner's position is that the disclosure does not provide a representative number of examples to demonstrate that the

claimed invention possessed the alleged utility and that the applicant had possession of the full scope of the claimed invention.

Solely to expedite prosecution of the application, Applicants have amended independent claims 32 and 42 to more particularly define the restriction sites of the claimed vector and the corresponding restriction enzymes. As amended, claim 32 recites "a recombinant vector comprising an isolated nucleotide sequence encoding an snRNA, wherein said nucleotide sequence has been modified to contain one or more restriction sites, such that digestion with a single restriction enzyme excises a restriction fragment which includes a restriction site for said restriction enzyme and forms insertion sites in said nucleotide sequence" (emphasis added). As amended, claim 42 recites a recombinant vector comprising an isolated nucleotide sequence encoding an snRNA, wherein said nucleotide sequence comprises an insertion cassette between two insertion sites, wherein said two insertion sites are formed by digestion with a single restriction enzyme to excise a restriction fragment that contains a restriction site for said restriction enzyme, and wherein said insertion cassette comprises a modification fragment comprising a nucleotide sequence complementary to a target" (emphasis added).

Applicants respectfully submit that the number of claimed nucleic acid sequences as amended is not very large because the restriction enzyme belongs to a unique family of restriction endonucleases that excise a fragment containing the recognition site.

Further, Applicants reiterate the arguments already made of record and contend that the pending claims meet the written description requirement. Applicants' invention is drawn to a vector containing a nucleotide sequence encoding an snRNA, which sequence has been modified to allow for excision of a restriction fragment and insertion of a nucleotide sequence complementary to a target sequence. The vector allows switching of target specificity of snRNAs with ease. At the time the invention was filed, a wide variety of appropriate vectors for use in the invention as claimed were well known in the art, and one of skill in the art would appreciate that vectors should be selected based in part on the particular use. Under the Guidelines for the Examination of Patent Applications Under the Written Description Requirement, 66 Fed. Reg. 1104, 1105 (Jan. 5, 2001), "[i]nformation which is well known in the art need not be described in detail in the specification." Accordingly, Applicants submit

that the pending claims are both enabled and supported by the specification of the application as filed. The Examiner has not overcome the "strong presumption that an adequate written description of the claimed invention is present" for an originally filed claim. Guidelines, p. 1105.

In view of the above amendments and arguments, Applicants submit that a skilled practitioner would conclude that Applicants had possession of the claimed invention at the time the application was filed. Accordingly, reconsideration and withdrawal of rejection are respectfully requested.

Claims Rejections Under 35 U.S.C. § 102(b)

Claims 32-34, 36, 41-42, 44-48, and 51 are rejected under 35 U.S.C. § 102(b) over Noonberg *et al.* (WO 95/10607). The Examiner states that Noonberg *et al.* disclose a recombinant vector comprising an isolated nucleotide sequence encoding a U6 snRNA, wherein the U6 snRNA vector has XhoI and NsiI restriction sites for inserting synthetic sequences.

Applicants submit that the pending claims, as amended, are novel over Noonberg *et al.* because Noonberg *et al.* neither teach nor suggest all the elements of the claimed invention.

As described above, claim 32 as amended is directed to a recombinant vector comprising an isolated nucleotide sequence encoding an snRNA, wherein said nucleotide sequence has been modified to contain one or more restriction sites, such that digestion with a single restriction enzyme excises a restriction fragment which contains a restriction site for said restriction enzyme and forms insertion sites in said nucleotide sequence.

In contrast, Noonberg *et al.* disclose a vector comprising two restriction sites of two different restriction enzymes (*e.g.*, XhoI and NsiI), and digesting the vector with two different restriction enzymes (see, *e.g.*, page 51, lines 3-7; Figure 4B). Further, the restriction fragment from the digestion would not contain the recognition sites for the restriction enzymes because the restriction enzymes (*e.g.*, XhoI and NsiI) cut within their recognition sites. Thus, Noonberg *et al.* fail to teach a vector as claimed in claim 32.

As described above, claim 42 as amended is directed to a recombinant vector comprising an isolated nucleotide sequence encoding an snRNA, wherein said nucleotide sequence comprises an insertion cassette between two insertion sites, wherein said two insertion sites are formed by digestion with a single restriction enzyme to excise a restriction fragment that contains a restriction site for said restriction enzyme, and wherein said insertion cassette comprises a modification fragment comprising a nucleotide sequence complementary to a target.

Although Noonberg *et al.* disclose insertion of an insertion cassette into their vector, the resultant construct would be different from the one as claimed in claim 42 because, as argued above, the Noonberg vector differs from the vector in claim 32 at least in the restriction site, restriction enzyme, and restriction fragment. Indeed, the invention of claim 42 is directed to a vector in which an insertion cassette is inserted at the restriction sites that are different from those in the Noonberg vector.

In sum, Applicants submit that independent claims 32 and 42, as well as claims dependent thereon, are novel and not obvious in view of the teachings of Noonberg *et al.* because Noonberg *et al.* do not teach or suggest all the elements of the invention of claims 32 and 42. Accordingly, reconsideration and withdrawal of the rejection are respectfully requested.

Claim Rejections Under 35 U.S.C. § 103(a)

Claims 32-51 are rejected under 35 U.S.C. § 103(a) over Noonberg *et al.* (WO 95/10607) in view of the alleged admission of prior art in the specification, Cohen *et al.* (Proc. Natl. Acad. Sci. 91: 10470-10474, 1994), Tuschl *et al.* (EMBO 17: 2637-2650, 1998), and Sears *et al.* (Nucl Acids Res 24: 3590-3592, 1996). Applicants respectfully traverse this rejection to the extent it is maintained over the claims as amended.

Pursuant to MPEP 2143 and in view of *In re* Vaeck, 947 F.2d 488, 20 USPQ2d 1438 (Fed. Cir. 1991), "[t]o establish a *prima facie* case of obviousness, three basic criteria must be met. First, there must be some suggestion or motivation, either in the references themselves or in the knowledge generally available to one of ordinary skill in the art, to modify the reference or to combine reference teachings. Second, there must be a reasonable expectation

of success. Finally, the prior art reference (or references when combined) must teach or suggest all the claim limitations."

Further, reliance on the specification as filed for providing motivation to combine the two references impermissible. M.P.E.P. § 706.02 (j) recites that "[t]he teaching or suggestion to make the claimed combination and the reasonable expectation of success must both be found in the prior art and not be based on applicant's disclosure. *In re* Vaeck, 947 F.2d 488, 20 USPQ2d 1438 (Fed. Cir. 1991)."

The Examiner first asserts that claims 32-34, 36, 41-42, 44-48, and 51 are obvious over Noonberg *et al.* in view of the alleged admission of prior art in the specification, Cohen *et al.*, and Tuschl *et al.* Applicants respectfully disagree.

Applicants submit that in view of the arguments presented above, Noonberg *et al.* do not teach all the elements of the claimed invention. Specifically, Noonberg *et al.* do not teach the restriction enzyme, restriction sites, or the restriction fragment in the vectors as recited in amended claims 32 and 42.

Cohen *et al.* teach site-directed mutagenesis of a vector comprising a U1 snRNA in pertinent parts (see Cohen *et al.*, Material and Methods). However, Cohen *et al.* do not teach or suggest the restriction enzyme, restriction sites, or the restriction fragment as recited in claims 32 and 42.

Tuschl *et al.* disclose a vector comprising two snRNAs (U2 and U6) contained between two restriction sites, and digesting the vector with two different restriction enzymes (*e.g.*, StyI and BanI). Further, the restriction fragment produced from the digestion would not contain the recognition sites for these restriction enzymes because the restriction enzymes (*e.g.*, StyI and BanI) cut within their recognition sites. Thus, Tuschl *et al.* do not teach the restriction enzyme, restriction sites, or the restriction fragment as recited in amended claims 32 and 42.

Therefore, Applicants submit that none of Noonberg *et al.*, Cohen *et al.*, and Tuschl *et al.* teach or suggest all the claim limitations. Even if combined, Noonberg *et al.*, Cohen *et al.*, and Tuschl *et al.* do not teach all the elements of the invention of claim 32 or 42. Further,

Applicants respectfully submit that the cited references, taken singly or in combination, do not provide an incentive or motivation to make the combination. Thus, at least two requirements for establishing a *prima facie* case of obviousness have not been satisfied. Accordingly, Applicants respectfully request reconsideration and withdrawal of the rejection of claims 32-34, 36, 41-42, 44-48, and 51 under 35 U.S.C. 103(a).

The Examiner further asserts that claims 37-40 and 49-50 are obvious over Noonberg *et al.* in view of the alleged admission of prior art in the specification, Cohen *et al.*, Tuschl *et al.*, and Sears *et al.* The Examiner acknowledges that Noonberg *et al.*, Cohen *et al.*, Tuschl *et al.*, and the alleged admission of prior art in the specification do not explicitly disclose the restriction enzyme, BaeI, restriction sites or restriction fragment containing the restriction site (see claims 32 and 42). However, the Examiner cited Sears *et al.* to establish a *prima facie* case of obviousness. Applicants respectfully disagree.

As described above, neither Cohen *et al.* nor Tuschl *et al.* teach the restriction enzyme, restriction sites, or the restriction fragment containing the restriction site (see claims 32 and 42).

Sears *et al.* disclose identification and characterization of a restriction enzyme, BaeI, which cuts double-stranded DNA on both strands upstream and downstream of it recognition site. However, Sears *et al.* do not teach or suggest use of the BaeI enzyme or similar enzymes in making the vector encoding an snRNA as recited in claims 32 or 42.

Applicants respectfully submit that the cited references, taken singly or in combination, do not provide an incentive or motivation to make the combination. Sears *et al.* at most indicate that the BaeI restriction enzyme and restriction site were available to make vectors at the time the application was filed. However, none of the other citations (Noonberg *et al.*, Cohen *et al.*, and Tuschl *et al.*) provide a motivation to use the teachings of Sears *et al.* to arrive at the claimed invention. Thus, at least one requirement for establishing a *prima facie* case of obviousness has not been satisfied. Accordingly, Applicants respectfully request reconsideration and withdrawal of the rejection of claims 37-40 and 49-50 under 35 U.S.C. 103(a).

CONCLUSION

In view of the foregoing amendments and remarks, the pending claims are in condition for allowance. Early and favorable reconsideration is respectfully solicited. The Examiner may address any questions raised by this submission to the undersigned at 617-951-7000. Should an extension of time be required, Applicants hereby petition for same and request that the extension fee and any other fee required for timely consideration of this submission be charged to **Deposit Account No. 18-1945, under Order No. WIBL-P01-523.**

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Respectfully submitted,

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